A.)

signal sequence

cysteine-rich

transmembrane domain

tyrosine kinase domain

P P P P P P

N — C EGFR wt

N — C mutated EGFR-II

Δ 25-312   Δ 679-1210

B.)

Ig-like domain   C6-box

tyrosine kinase domain

N — C wt MuSK

N — C mutated MuSK

Δ 587-869

FIGURE 1

```
    MRPSGTAGAA LLALLAALCP ASRALEEKKV CQGTSNKLTQ LGTFEDHFLS        50
    LQRMFNNCEV VLGNLEITYV QRNYDLSFLK TIQEVAGYVL IALNTVERIP       100
    LENLQIIRGN MYYENSYALA VLSNYDANKT GLKELPMRNL QEILHGAVRF       150
    SNNPALCNVE SIQWRDIVSS DFLSNMSMDF QNHLGSCQKC DPSCPNGSCW       200
  5 GAGEENCQKL TKIICAQQCS GRCRGKSPSD CCHNQCAAGC TGPRESDCLV       250
    CRKFRDEATC KDTCPPLMLY NPTTYQMDVN PEGKYSFGAT CVKKCPRNYV       300
    VTDHGSCVRA CGADSYEMEE DGVRKCKKCE GPCRKVCNGI GIGEFKDSLS       350
    INATNIKHFK NCTSISGDLH ILPVAFRGDS FTHTPPLDPQ ELDILKTVKE       400
    ITGFLLIQAW PENRTDLHAF ENLEIIRGRT KQHGQFSLAV VSLNITSLGL       450
 10 RSLKEISDGD VIISGNKNLC YANTINWKKL FGTSGQKTKI ISNRGENSCK       500
    ATGQVCHALC SPEGCWGPEP RDCVSCRNVS RGRECVDKCN LLEGEPREFV       550
    ENSECIQCHP ECLPQAMNIT CTGRGPDNCI QCAHYIDGPH CVKTCPAGVM       600
    GENNTLVWKY ADAGHVCHLC HPNCTYGCTG PGLEGCPTNG PKIPSIATGM       650
    VGALLLLLVV ALGIGLFMRR RHIVRKRTLR RLLQERELVE PLTPSGEAPN       700
 15 QALLRILKET EFKKIKVLGS GAFGTVYKGL WIPEGEKVKI PVAIKELREA       750
    TSPKANKEIL DEAYVMASVD NPHVCRLLGI CLTSTVQLIT QLMPFGCLLD       800
    YVREHKDNIG SQYLLNWCVQ IAKGMNYLED RRLVHRDLAA RNVLVKTPQH       850
    VKITDFGLAK LLGAEEKEYH AEGGKVPIKW MALESILHRI YTHQSDVWSY       900
    GVTVWELMTF GSKPYDGIPA SEISSILEKG ERLPQPPICT IDVYMIMVKC       950
 20 WMIDADSRPK FRELIIEFSK MARDPQRYLV IQGDERMHLP SPTDSNFYRA      1000
    LMDEEDMDDV VDADEYLIPQ QGFFSSPSTS RTPLLSSLSA TSNNSTVACI      1050
    DRNGLQSCPI KEDSFLQRYS SDPTGALTED SIDDTFLPVP EYINQSVPKR      1100
    PAGSVQNPVY HNQPLNPAPS RDPHYQDPHS TAVGNPEYLN TVQPTCVNST      1150
    FDSPAHWAQK GSHQISLDNP DYQQDFFPKE AKPNGIFKGS TAENAEYLRV      1200
 25 APQSSEFIGA                                                   1210
```

FIGURE 2

```
     ATGCGACCCT  CCGGGACGGC  CGGGGCAGCG  CTCCTGGCGC  TGCTGGCTGC      50

     GCTCTGCCCG  GCGAGTCGGG  CTCTGGAGGA  AAAGAAAGTT  TGCCAAGGCA     100

     CGAGTAACAA  GCTCACGCAG  TTGGGCACTT  TTGAAGATCA  TTTTCTCAGC     150

  5  CTCCAGAGGA  TGTTCAATAA  CTGTGAGGTG  GTCCTTGGGA  ATTTGGAAAT     200

     TACCTATGTG  CAGAGGAATT  ATGATCTTTC  CTTCTTAAAG  ACCATCCAGG     250

     AGGTGGCTGG  TTATGTCCTC  ATTGCCCTCA  ACACAGTGGA  GCGAATTCCT     300

     TTGGAAAACC  TGCAGATCAT  CAGAGGAAAT  ATGTACTACG  AAAATTCCTA     350

     TGCCTTAGCA  GTCTTATCTA  ACTATGATGC  AAATAAAACC  GGACTGAAGG     400

 10  AGCTGCCCAT  GAGAAATTTA  CAGGAAATCC  TGCATGGCGC  CGTGCGGTTC     450

     AGCAACAACC  CTGCCCTGTG  CAACGTGGAG  AGCATCCAGT  GGCGGGACAT     500

     AGTCAGCAGT  GACTTTCTCA  GCAACATGTC  GATGGACTTC  CAGAACCACC     550

     TGGGCAGCTG  CCAAAAGTGT  GATCCAAGCT  GTCCCAATGG  GAGCTGCTGG     600

     GGTGCAGGAG  AGGAGAACTG  CCAGAAACTG  ACCAAAATCA  TCTGTGCCCA     650

 15  GCAGTGCTCC  GGGCGCTGCC  GTGGCAAGTC  CCCCAGTGAC  TGCTGCCACA     700

     ACCAGTGTGC  TGCAGGCTGC  ACAGGCCCCC  GGGAGAGCGA  CTGCCTGGTC     750

     TGCCGCAAAT  TCCGAGACGA  AGCCACGTGC  AAGGACACCT  GCCCCCCACT     800

     CATGCTCTAC  AACCCCACCA  CGTACCAGAT  GGATGTGAAC  CCCGAGGGCA     850

     AATACAGCTT  TGGTGCCACC  TGCGTGAAGA  AGTGTCCCCG  TAATTATGTG     900

 20  GTGACAGATC  ACGGCTCGTG  CGTCCGAGCC  TGTGGGGCCG  ACAGCTATGA     950

     GATGGAGGAA  GACGGCGTCC  GCAAGTGTAA  GAAGTGCGAA  GGGCCTTGCC    1000

     GCAAAGTGTG  TAACGGAATA  GGTATTGGTG  AATTTAAAGA  CTCACTCTCC    1050

     ATAAATGCTA  CGAATATTAA  ACACTTCAAA  AACTGCACCT  CCATCAGTGG    1100

     CGATCTCCAC  ATCCTGCCGG  TGGCATTTAG  GGGTGACTCC  TTCACACATA    1150

 25  CTCCTCCTCT  GGATCCACAG  GAACTGGATA  TTCTGAAAAC  CGTAAAGGAA    1200

     ATCACAGGGT  TTTTGCTGAT  TCAGGCTTGG  CCTGAAAACA  GGACGGACCT    1250

     CCATGCCTTT  GAGAACCTAG  AAATCATACG  CGGCAGGACC  AAGCAACATG    1300

     GTCAGTTTTC  TCTTGCAGTC  GTCAGCCTGA  ACATAACATC  CTTGGGATTA    1350

     CGCTCCCTCA  AGGAGATAAG  TGATGGAGAT  GTGATAATTT  CAGGAAACAA    1400

 30
```

FIGURE 3A

```
      AAATTTGTGC TATGCAAATA CAATAAACTG GAAAAAACTG TTTGGGACCT        1450
      CCGGTCAGAA AACCAAAATT ATAAGCAACA GAGGTGAAAA CAGCTGCAAG        1500
      GCCACAGGCC AGGTCTGCCA TGCCTTGTGC TCCCCCGAGG GCTGCTGGGG        1550
 5    CCCGGAGCCC AGGGACTGCG TCTCTTGCCG GAATGTCAGC CGAGGCAGGG        1600
      AATGCGTGGA CAAGTGCAAG CTTCTGGAGG GTGAGCCAAG GGAGTTTGTG        1650
      GAGAACTCTG AGTGCATACA GTGCCACCCA GAGTGCCTGC CTCAGGCCAT        1700
      GAACATCACC TGCACAGGAC GGGGACCAGA CAACTGTATC CAGTGTGCCC        1750
      ACTACATTGA CGGCCCCCAC TGCGTCAAGA CCTGCCCGGC AGGAGTCATG        1800
10    GGAGAAAACA ACACCCTGGT CTGGAAGTAC GCAGACGCCG GCCATGTGTG        1850
      CCACCTGTGC CATCCAAACT GCACCTACGG ATGCACTGGG CCAGGTCTTG        1900
      AAGGCTGTCC AACGAATGGG CCTAAGATCC CGTCCATCGC CACTGGGATG        1950
      GTGGGGGCCC TCCTCTTGCT GCTGGTGGTG GCCCTGGGGA TCGGCCTCTT        2000
      CATGCGAAGG CGCCACATCG TTCGGAAGCG CACGCTGCGG AGGCTGCTGC        2050
15    AGGAGAGGGA GCTTGTGGAG CCTCTTACAC CCAGTGGAGA AGCTCCCAAC        2100
      CAAGCTCTCT TGAGGATCTT GAAGGAAACT GAATTCAAAA AGATCAAAGT        2150
      GCTGGGCTCC GGTGCGTTCG GCACGGTGTA TAAGGGACTC TGGATCCCAG        2200
      AAGGTGAGAA AGTTAAAATT CCCGTCGCTA TCAAGGAATT AAGAGAAGCA        2250
      ACATCTCCGA AAGCCAACAA GGAAATCCTC GATGAAGCCT ACGTGATGGC        2300
20    CAGCGTGGAC AACCCCCACG TGTGCCGCCT GCTGGGCATC TGCCTCACCT        2350
      CCACCGTGCA ACTCATCACG CAGCTCATGC CCTTCGGCTG CCTCCTGGAC        2400
      TATGTCCGGG AACACAAAGA CAATATTGGC TCCCAGTACC TGCTCAACTG        2450
      GTGTGTGCAG ATCGCAAAGG GCATGAACTA CTTGGAGGAC CGTCGCTTGG        2500
      TGCACCGCGA CCTGGCAGCC AGGAACGTAC TGGTGAAAAC ACCGCAGCAT        2550
25    GTCAAGATCA CAGATTTTGG GCTGGCCAAA CTGCTGGGTG CGGAAGAGAA        2600
      AGAATACCAT GCAGAAGGAG GCAAAGTGCC TATCAAGTGG ATGGCATTGG        2650
      AATCAATTTT ACACAGAATC TATACCCACC AGAGTGATGT CTGGAGCTAC        2700
      GGGGTGACCG TTTGGGAGTT GATGACCTTT GGATCCAAGC CATATGACGG        2750
      AATCCCTGCC AGCGAGATCT CCTCCATCCT GGAGAAAGGA GAACGCCTCC        2800
30
```

FIGURE 3B
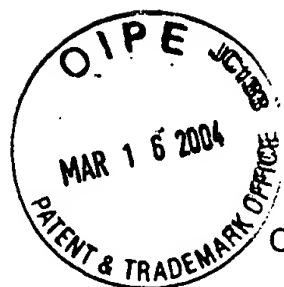
```
   CTCAGCCACC CATATGTACC ATCGATGTCT ACATGATCAT GGTCAAGTGC        2850

   TGGATGATAG ACGCAGATAG TCGCCCAAAG TTCCGTGAGT TGATCATCGA        2900

   ATTCTCCAAA ATGGCCCGAG ACCCCCAGCG CTACCTTGTC ATTCAGGGGG        2950

   ATGAAAGAAT GCATTTGCCA AGTCCTACAG ACTCCAACTT CTACCGTGCC        3000

 5 CTGATGGATG AAGAAGACAT GGACGACGTG GTGGATGCCG ACGAGTACCT        3050

   CATCCCACAG CAGGGCTTCT TCAGCAGCCC CTCCACGTCA CGGACTCCCC        3100

   TCCTGAGCTC TCTGAGTGCA ACCAGCAACA ATTCCACCGT GGCTTGCATT        3150

   GATAGAAATG GGCTGCAAAG CTGTCCCATC AAGGAAGACA GCTTCTTGCA        3200

   GCGATACAGC TCAGACCCCA CAGGCGCCTT GACTGAGGAC AGCATAGACG        3250

10 ACACCTTCCT CCCAGTGCCT GAATACATAA ACCAGTCCGT TCCCAAAAGG        3300

   CCCGCTGGCT CTGTGCAGAA TCCTGTCTAT CACAATCAGC CTCTGAACCC        3350

   CGCGCCCAGC AGAGACCCAC ACTACCAGGA CCCCCACAGC ACTGCAGTGG        3400

   GCAACCCCGA GTATCTCAAC ACTGTCCAGC CCACCTGTGT CAACAGCACA        3450

   TTCGACAGCC CTGCCCACTG GGCCCAGAAA GGCAGCCACC AAATTAGCCT        3500

15 GGACAACCCT GACTACCAGC AGGACTTCTT TCCCAAGGAA GCCAAGCCAA        3550

   ATGGCATCTT TAAGGGCTCC ACAGCTGAAA ATGCAGAATA CCTAAGGGTC        3600

   GCGCCACAAA GCAGTGAATT TATTGGAGCA TGA                         3630
```

20

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FIGURE 3C

First PCR Reaction

EGFR1 + EGFR3   primer

a.) ═══ EGFR cDNA

═══ PCR product a
encoding aa 1 to 24 fused to aa 313 to 319

EGFR2   +   EGFR2220R   primer

b.) ═══ EGFR cDNA

═══════════════ PCR product b
encoding aa 18 to 24 fused to aa 313 to 678

Second PCR Reaction

═══════════════ PCR product a + b

a.) ──────────── overlap extension

═══════════════ PCR product c
encoding aa 1 to 24 fused to aa 313 to 678
with a stop codon in position 679

EGFR1   +   EGFR2220R   primer
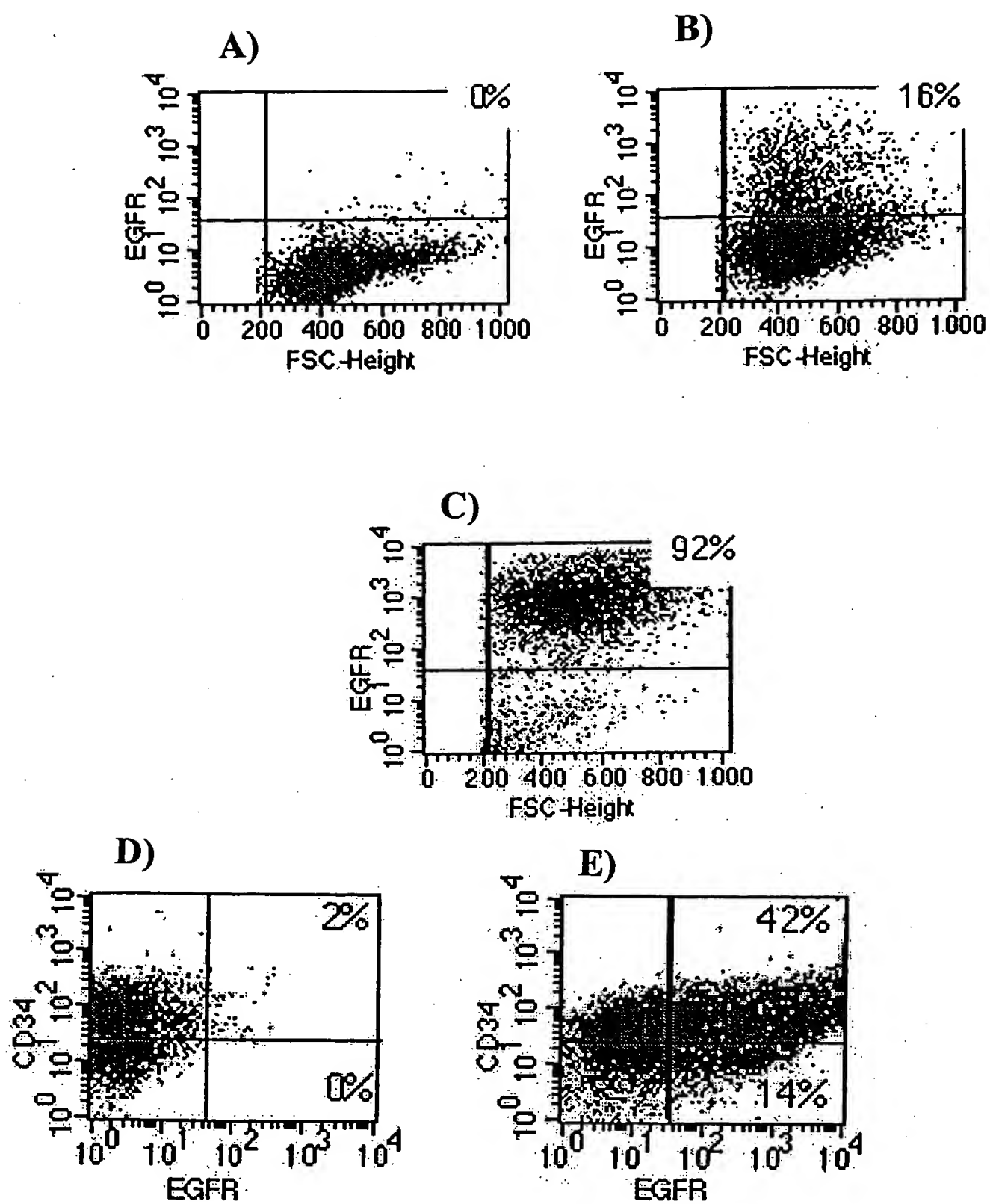
b.) ═══════════════ amplification of
PCR product c

FIGURE 4

FIGURE 5